DEPARTMENT OF HEALTH & HUMAN SERVICES

MAY 22 2009

Food and Drug Administration
Rockville MD 20857

Rec'd MB 6.9.09

Gary Lamoureux
World Wide Medical Technologies
115 Hurley Road, Building 3B
Oxford, CT 06478

Re: Docket No. 2005P-0084

Dear Mr. Lamoureux:

This letter responds to your citizen petition dated February 18, 2005, and filed by the Food and Drug Administration (FDA) on February 23, 2005. Your petition requests that FDA ban or require premarket approval applications (PMA) for brachytherapy kits for treatment of prostate cancer (prostate brachytherapy kits) that use "non-absorbable bone wax or reformulated 'faux bone wax' needle plugs."[1] We provided to you an interim response on August 16, 2005, stating that we needed additional time to review your petition. We have completed our review and are denying your petition. Below we summarize your petition and provide the bases for our denial.

A. Summary of the Citizen Petition

In your petition, you ask FDA to safeguard the public from non-absorbable bone wax or non-absorbable reformulated "faux bone wax"[2] needle plugs used in brachytherapy kits that are intended for use in the treatment of prostate cancer. As you describe, such a kit consists of a needle pre-loaded with radioactive brachytherapy seeds and accompanying spacers, with a bone wax needle plug that retains the seeds inside the needle prior to insertion.[3] You assert that because multiple needles are used in the course of a single patient's brachytherapy, in total, brachytherapy kits permanently implant a "substantial" amount of non-absorbable bone wax or reformulated "faux bone wax" into soft tissue.[4]

You state that scientific data published in journals from the fields of orthopedic, mastoid, thoracic, cardiac, foot, plastic, ophthalmic, and dental surgery indicate that the migration of bone wax from surgical bone sites into areas of soft tissue within the body can potentially lead to serious complications, including sarcoma, chronic inflammation, foreign body reaction, epistaxis, allergic reaction, sigmoid sinus thrombosis, foreign body

[1] World Wide Medical Technologies Citizen Petition ("Citizen Petition"), page 3.
[2] In your petition, you allege generally that some commercial prostate brachytherapy kits may be using "faux bone wax" material for needle plugs, but you do not provide specific information about which products you believe use such novel materials. Your attached lab report does not establish what the source of the material tested was. We are not familiar with the term "faux bone wax" mentioned in your petition, but we note that not all of the formulations of bone wax cleared for use in hemostasis use bees' wax as their main constituent.
[3] Citizen Petition, page 4.
[4] Citizen Petition, pages 4, 12.

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venous embolization, pulmonary complications from migration to the lungs, and quadriplegia.[5]

You state that although health care professionals have used bone wax for needle plugs when loading individual brachytherapy prescriptions, you found no studies that address bone wax migration or the mid- to long-term effects of bone wax residing in soft tissue.[6] You indicate that bone wax used as needle plugs was developed for use as a hemostasis agent in bone and, to the best of your knowledge, has only been cleared by FDA to stop bone bleeding locally.[7] While you do not ask FDA to take action regarding legally marketed bone wax labeled for use in hemostasis and specifically indicate that your petition "is not intended to affect brachytherapy systems assembled by medical professionals prior to performing brachytherapy surgery,"[8] you contend that commercial brachytherapy kits for the treatment of prostate cancer that include needle plugs made of non-absorbable bone wax or "faux bone wax" warrant increased regulatory oversight.

In your petition, you specifically request that:

(1) FDA ban the use of prostate brachytherapy kits that use non-absorbable bone wax or reformulated "faux bone wax" needle plugs, under section 516(a)(1) of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. 360(f)(a)(1)), because they present an "unreasonable and substantial risk of illness or injury;" or

(2) FDA require all manufacturers of prostate brachytherapy kits that use bone wax or reformulated "faux bone wax" needle plugs to obtain FDA approval of a premarket approval application (PMA) prior to commercial distribution; and

(3) Regardless of whether FDA decides to ban brachytherapy kits that use bone wax or reformulated faux bone wax kits, or require PMAs, FDA also rescind any current "substantial equivalence" orders for such kits and remove from the market any prostate brachytherapy kits that use bone wax needle plugs marketed in the absence of 510(k) clearance or approval.

B. Bases for Denial

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[5] Citizen Petition, pages 1-3.
[6] Citizen Petition, pages 4-5.
[7] Citizen Petition, page 17.
[8] Citizen Petition, page 3, n. 8. Practitioners preparing individual brachytherapy doses using cleared brachytherapy sources and separately-cleared needles have for many years used substances including bone wax to plug those needles to prevent loss of the radioactive seeds between loading and insertion into the patient. Several stand-alone brachytherapy needles cleared by FDA, including one manufactured by your own company, include directions calling for the use of bone wax to plug the needle after loading. See, e.g., K974118 (SE January 23, 1998).

We have reviewed the information that you submitted with your petition, other published clinical literature, FDA's Medical Device Reporting (MDR) database, and other information regarding the components of cleared prostate brachytherapy kits through Spring 2009. Notably, your petition provides no evidence or data demonstrating that bone wax needle plugs, used in prostate brachytherapy kits, have caused any of the events your petition mentions. Rather, your petition appears based on your own hypotheses from literature and adverse events regarding bone wax used in hemostasis to control bleeding from bone surfaces, and not on literature or adverse events regarding bone wax used as needle plugs in prostate brachytherapy kits. As discussed below, we do not consider hemostatic adverse events involving bone wax to be relevant in the context of needle plugs made of bone wax for brachytherapy treatment.

The lack of evidence in your petition related to bone wax needle plugs used in prostate brachytherapy kits, mirrors the conclusion of our own review of the published literature and FDA's MDR database: we are not aware of any data linking bone wax needle plugs used in prostate brachytherapy kits, to any of the events your petition references. In fact, FDA has not received any reports of adverse events relating to bone wax needle plugs used in brachytherapy treatment. Accordingly, we have determined that there is no scientific basis to undertake the actions you request of either banning or requiring PMAs for this device, which remains as a treatment for a potentially life-threatening cancer.[9]

We conclude that there exists no scientific support for banning or requiring PMAs for prostate brachytherapy kits that use bone wax needle plugs. Brachytherapy kits are class II devices, under regulation 21 CFR 892.5730, Radionuclide brachytherapy source. For brachytherapy kits to be class II devices under 21 CFR 892.5730, they must be substantially equivalent to legally marketed predicate devices. See section 513(f)(1), 21 U.S.C. § 360(c)(f)(1).

Banning a device is required under 21 U.S.C. § 360f(a) when, on the basis of all available data and information, the device presents an unreasonable and substantial risk of illness or injury. Premarket approval for a device is required under 21 U.S.C. §360c(a)(1)(C), when there is insufficient information to determine that general and special controls would provide reasonable assurance of safety and effectiveness.

We have before us no evidence of harm attributable to bone wax needle plugs used in prostate brachytherapy kits, whether as part of commercial kits or through preparation by individual practitioners. Rather, your petition appears based on your speculative hypotheses that adverse events, such as foreign body reactions and migration, reported to have occurred where a substantial quantity of bone wax was used to control bleeding in bone, might also occur with brachytherapy kits that use a minimal quantity of bone wax for needle plugs.

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[9] Guideline for the Management of Clinically Localized Prostate Cancer: 2007 Update, by the American Urological Association Education and Research, Inc., in The Journal of Urology 2007; 177:2106-2131. The Guideline notes brachytherapy as a monotherapy treatment option for such patients. In addition, NICE in England (National Institute for Health and Clinical Excellence) published a Guidance in July 2005, stating that brachytherapy was effective for localized prostate cancer.

While you identify adverse events reported after use of bone wax to control bleeding in bone to suggest that there are inadequately controlled risks associated with prostate brachytherapy kits containing similar materials as components, in fact many of these reported events are potential reactions to the implant of *any* foreign body. However, neither your petition nor our literature review identified any data specifically addressing an increased incidence or severity in these side effects of implanted medical devices for bone wax needle plugs used in prostate brachytherapy kits.

You also contend that prostate brachytherapy kits containing bone wax needle plugs can cause harm requiring additional regulatory oversight because the radioactive seeds used in prostate brachytherapy can migrate from the treatment site, which you suggest indicates that bone wax needle plugs may also migrate.[10] You further speculate that such migration, if it occurred, could cause serious health problems, particularly if the plugs migrate to the lungs.[11] Again, you provide no specific evidence of bone wax needle plug migration or consequent health problems. In fact, migration to the lungs and other tissues is a possible but rare side effect of any injected material, including brachytherapy seeds themselves.

Significant differences between the use of bone wax to control bone bleeding and bone wax for needle plugs in brachytherapy kits, make the adverse events reported in the hemostatic context unlikely to occur in the prostate brachytherapy context. In orthopedic surgery, typically a large mass of bone wax is spread onto the cut surface of bone to achieve tamponade. In this use, if excess bone wax is not removed from the site of application, a large mass of it may become displaced. Depending on the excess bone wax's original location, it may contribute to certain adverse events reported in the literature you cite, and because it is not confined within an organ, its ability to move into a problematic area increases.[12] By contrast, in prostate brachytherapy, not only is the total amount of bone wax used substantially less than the amount used in most bone hemostasis applications, but, also, each individual needle plug is placed in a distinct, separate location within the prostate, where the individual needle plugs are unlikely to aggregate and migrate as a larger mass. Moreover, FDA's searches for evidence in the published literature and MDR database, which include reports from manufacturers, importers, user facilities, and consumers, identified no reports of either bone wax needle plug migration, or any adverse events associated with bone wax needle plugs used in prostate brachytherapy, in their original placement.

C. Conclusions

[10] Citizen Petition, page 5, 12.

[11] Citizen Petition, page 5.

[12] For example, the literature you provided and other information we reviewed indicates that quadriplegia after use of bone wax has been observed in one isolated case of a spinal surgery where large amounts of bone wax were used to control bleeding and excess bone wax was not removed from the spinal surgical site. See Citizen Petition, pages 9-10. Surgeons consequently conjectured that the patient's subsequent quadriplegia might be the result of excess bone wax compressing the spinal cord.

1. Based on all available data and information, FDA is denying your request that FDA ban prostate brachytherapy kits that use bone wax needle plugs.

On the basis of the foregoing and all available data and information, supplied by you and acquired through our own review, we cannot conclude that prostate brachytherapy kits with bone wax needle plugs present an unreasonable and substantial risk of illness or injury. Therefore, banning these devices is unwarranted. See 21 U.S.C. § 360f(a).

2. Based on all available data and information, FDA is denying your request to require PMAs for prostrate brachytherapy kits that use bone wax needle plugs.

On the basis of the foregoing and all available data and information, supplied by you and acquired through our own review, we conclude that the current general and special controls, which include premarket notifications, good manufacturing practices, adverse event reporting, and appropriate labeling, applicable to all cleared prostate brachytherapy devices, including those that have a bone wax needle plug and those that require the user to supply one, typically expected to be bone wax, provide a reasonable assurance of the safety and effectiveness of those devices. See 21 U.S.C. § 360c(a). Therefore, reclassifying prostate brachytherapy kits that include bone wax needle plugs under 21 U.S.C. §360c(e), into Class III and requiring a PMA is not warranted. Brachytherapy kits substantially equivalent to legally marketed predicate devices remain class II devices, under the regulation 21 CFR 892.5730, Radionuclide brachytherapy source.

3. Based on all available data and information, FDA is denying your request to rescind the determinations of "substantial equivalence" for cleared prostrate brachytherapy kits that use bone wax needle plugs.

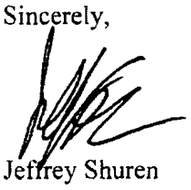
On the basis of the foregoing and all available data and information, supplied by you and acquired through our own review, we conclude that no basis exists for rescinding the determinations of substantial equivalence for cleared prostate brachytherapy kits that use bone wax needle plugs.[13]

While we decline to take the regulatory actions regarding bone wax needle plugs in prostate brachytherapy kits requested in your petition, you also state in your petition that, "[t]here are a number of companies advertising commercial brachytherapy kits that promote the use of . . . reformulated 'faux bone wax' plugs."[14] Therefore, if you are aware of prostate brachytherapy devices that you believe to be illegally marketed without premarket clearance or approval, we ask that you please provide any information you have to the Center for Devices and Radiological Health's Office of Compliance, at (240) 276-0115. To the extent you are petitioning the agency to take a particular enforcement

[13] The Citizen Petition, at page 19, relies on a proposed rule, 66 Federal Register 3523 (Jan. 16, 2001), which was withdrawn. See 67 FR 33039, 33046 (May 13, 2002).
[14] Citizen Petition, page 17.

action, however, we are denying that request since a person may not petition the agency for enforcement action through the citizen petition process. 21 CFR 10.30(k). If you have any questions regarding this response, please contact Heather Rosecrans, Director, 510(k) Staff, at (240) 276-4021.

Sincerely,



Jeffrey Shuren
Associate Commissioner for
Policy and Planning